(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

07 OCT 2004

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
23 October 2003 (23.10.2003)

PCT

(10) International Publication Number
WO 2003/087115 A3

(51) International Patent Classification[7]: A61K 48/00, C07H 21/04

(21) International Application Number: PCT/US2003/010840

(22) International Filing Date: 9 April 2003 (09.04.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
10/119,432 9 April 2002 (09.04.2002) US

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(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*
— *with amended claims and statement*

(88) Date of publication of the international search report:
4 November 2004

Date of publication of the amended claims and statement:
16 December 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2003/087115 A3

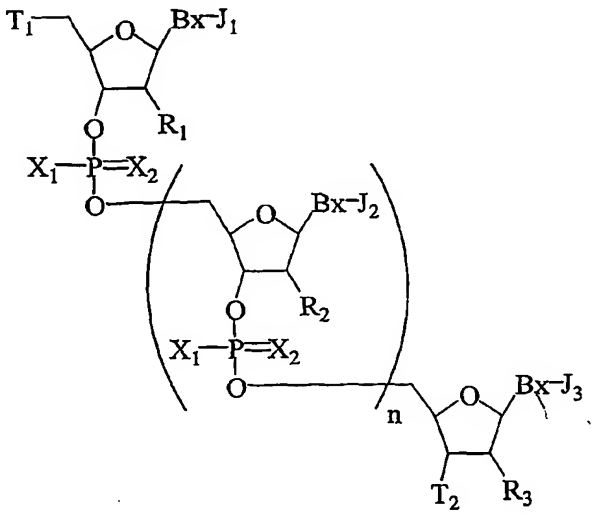
(54) Title: OLIGOMERIC COMPOUNDS HAVING MODIFIED PHOSPHATE GROUPS

(57) Abstract: Oligomeric compounds having at least one phosphorothioate monoester are provided having increased nuclease resistance and binding affinity to a complementary strand of nucleic acid. Such oligomeric compounds are useful for diagnostics and other research purposes, for modulating the expression of a protein in organisms, and for the diagnosis, detection and treatment of other conditions responsive to oligonucleotide therapeutics.

AMENDED CLAIMS

**[Received by the International Bureau on 06 October 2004 (06.10.04)
original claims 1 and 24 amended;
remaining claims unchanged (8 pages)].**

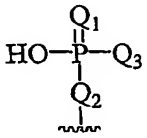
1 (amended). An oligomeric compound having the formula:



wherein:

each Bx is, independently, a heterocyclic base moiety;

J_1, J_3 and each J_2 is, independently, hydrogen or a modified phosphate group having the structure:



wherein

one of Q_1 and Q_2 is S and the other of Q_1 and Q_2 is O;

Q_3 is OH or CH_3;

R_1, R_3 and each R_2 is, independently, hydrogen, hydroxyl, a sugar substituent group a protected sugar substituent group or said modified phosphate group;

each T_1 and T_2 is, independently, hydroxyl, a protected hydroxyl, an oligonucleotide, an oligonucleoside or said modified phosphate group;

each X_1 and X_2 is, independently, O or S wherein at least one X_1 is S;

n is from 3 to 48; and

wherein at least one of J_1, J_2, J_3, ~~R_1, R_2, R_3,~~ T_1 or T_2 is said modified phosphate group.

2 (original). The oligomeric compound of claim 1 wherein Q_1 is S.

3 (original). The oligomeric compound of claim 1 wherein Q_2 is S.

4 (original). The oligomeric compound of claim 1 wherein Q_3 is CH_3.

5 (original). The oligomeric compound of claim 1 wherein J_1 is said modified phosphate group.

6 (original). The oligomeric compound of claim 1 wherein at least one J_2 is said modified phosphate group.

7 (original). The oligomeric compound of claim 1 wherein J_3 is said modified phosphate group.

8 (original) The oligomeric compound of claim 1 wherein R_1 is a modified phosphate group.

9 (original). The oligomeric compound of claim 1 wherein at least one R_2 is a modified phosphate group.

10 (original). The oligomeric compound of claim 1 wherein R_3 is a modified phosphate group.

11 (original). The oligomeric compound of claim 1 wherein R_1, R_3 and each R_2 is hydrogen.

12 (original). The oligomeric compound of claim 1 wherein R_1, R_3 and each R_2 is hydroxyl.

13 (original). The oligomeric compound of claim 1 wherein R_1, R_3 and each R_2 is hydrogen, hydroxyl a sugar substituent group or a protected sugar substituent group.

14 (original). The oligomeric compound of claim 1 wherein at least one of R_1, R_2 or R_3 is an optionally protected sugar substituent group.

15 (original). The oligomeric compound of claim 1 wherein each X_2 is S.

16 (original). The oligomeric compound of claim 1 wherein each heterocyclic base moiety is, independently, adenine, cytosine, 5-methylcytosine, thymine, uracil, guanine or 2-aminoadenine.

17 (original). The oligomeric compound of claim 1 wherein n is from about 8 to about 30.

18 (original). The oligomeric compound of claim 1 wherein n is from about 15 to 25.

19 (original). A method of treating an organism having a disease characterized by the undesired production of a protein comprising contacting the organism with an oligomeric compound of claim 1.

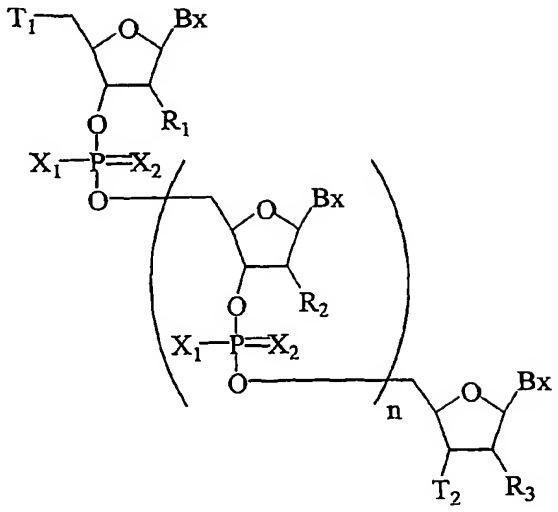
20 (original). A pharmaceutical composition comprising:
a pharmaceutically effective amount of an oligomeric compound of claim 1; and
a pharmaceutically acceptable diluent or carrier.

21 (original). A method of modifying *in vitro* a nucleic acid, comprising contacting a test solution containing RNase H and said nucleic acid with an oligomeric compound of claim 1.

22 (original). A method of concurrently enhancing hybridization and RNase H activation in a organism comprising contacting the organism with an oligomeric compound of claim 1.

23 (original). A method comprising contacting a cell with an oligomeric compound of claim 1.

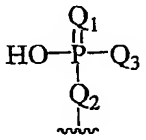
24 (currently amended). An oligomeric compound having the formula:



wherein

each Bx is, independently, a heterocyclic base moiety;

each T_1 and T_2 is, independently, hydroxyl, a protected hydroxyl, an oligonucleotide, an oligonucleoside or a modified phosphate group having the formula;



wherein

one of Q_1 and Q_2 is S and the other of Q_1 and Q_2 is O;

Q_3 is OH or CH_3;

R_1, R_3 and each R_2 is, independently, hydrogen, hydroxyl, a sugar substituent group, or a protected sugar substituent group;

each X_1 and X_2 is, independently, O or S wherein at least one X_1 is S; and

n is from 3 to 48;

wherein at least one of X_1, X_2, J_1, J_2, and J_3 is said modified phosphate group.

25 (original). The oligomeric compound of claim 24 wherein Q_1 is S.

26 (original). The oligomeric compound of claim 24 wherein Q_2 is S.

27 (original). The oligomeric compound of claim 24 wherein Q_3 is CH_3.

28 (original). The oligomeric compound of claim 24 wherein J_1 is said modified phosphate group.

29 (original). The oligomeric compound of claim 24 wherein at least one J_2 is a modified phosphate group.

30 (original). The oligomeric compound of claim 24 wherein J_3 is said modified phosphate group.

31 (original). The oligomeric compound of claim 24 wherein R_1 is a modified phosphate group.

32 (original). The oligomeric compound of claim 24 wherein at least one R_2 is a modified phosphate group.

33 (original). The oligomeric compound of claim 24 wherein R_3 is a modified phosphate group.

34 (original). The oligomeric compound of claim 24 wherein R_1, R_3 and each R_2 is hydrogen.

35 (original). The oligomeric compound of claim 24 wherein R_1, R_3 and each R_2 is hydroxyl.

36 (original). The oligomeric compound of claim 24 wherein R_1, R_3 and each R_2 is hydrogen, hydroxyl a sugar substituent group or a protected sugar substituent group.

37 (original). The oligomeric compound of claim 24 wherein at least one of R_1, R_2 or R_3 is an optionally protected sugar substituent group.

38 (original). The oligomeric compound of claim 24 wherein each X_2 is S.

39 (original). The oligomeric compound of claim 24 wherein each heterocyclic base moiety is, independently, adenine, cytosine, 5-methylcytosine, thymine, uracil, guanine or 2-aminoadenine.

40 (original). The oligomeric compound of claim 24 wherein n is from about 8 to about 30.

41 (original). The oligomeric compound of claim 24 wherein n is from about 15 to 25.

STATEMENT UNDER PCT ARTICLE 19

In response to the International Search Report mailed 10 September 2004, for the above-identified International Patent Application, enclosed is an Amendment Under Article 19. Sheets numbered 96 and 99 are enclosed to replace originally submitted sheets 96 and 99 of the claims.

Claims 1 and 24 are amended in the replacement sheets. The basis for the amendments can be found, for example, at page 10, lines 5-7 of the paragraph immediately above paragraph 26.